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10/764,691

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Gary L. Bowlin

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EXAMINER

SINGH, SATYENDRA K

ART UNIT

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1657

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|---------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/764,691 | Applicant(s) BOWLIN ET AL. | |
| | Examiner SATYENDRA K. SINGH | Art Unit 1657 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-22 is/are pending in the application.
- 4a) Of the above claim(s) 3,6-20 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,5 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 July 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/11/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

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vDETAILED ACTION

Applicant's submission filed on November 17th 2008 (and IDS filed on 12/11/2008) has been entered.

Claims 3, 6-20 and 22 (groups II-VII) remain withdrawn from further consideration.

Claim 2 has been previously canceled by applicants.

Claims 1, 4, 5, and 21 (group I; as currently amended) are examined on their merits in this office action.

The following contains new grounds of rejection necessitated by applicant's current amendments to the pending claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1 Claims 1, 4, 5 and 21 (as currently amended) are/**remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Coffee RA (WO 98/03267; IDS, citation # 70) taken with Coffee RA

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(US 2001/0003148; IDS, citation # 1) and Coffee RA (US 6,252,129; IDS, citation No. 46), and further in view of Weinberg (US 4,837,379; [A]).

Claims are directed to “Electrodeposited fibrin matrix with cells”, wherein the cells are delivered to the matrix during fabrication of the electrodeposited fibrin matrix upon a target that contains calcium, wherein the cells are suspended in a solution comprising molecules capable of forming fibrin during delivery to the matrix (or wherein the cells are entrapped within the matrix during fabrication of the electrodeposited fibrin matrix upon a target that contains calcium), wherein the cells are suspended in a fibrinogen solution during delivery to the matrix, and wherein a cross-linking agent is added to the electrodeposited fibrin matrix (see instant claims 1, and 21 as currently amended).

*"[E]ven though **product-by-process** claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).*

Coffee RA (WO 98/03267, IDS) discloses electrohydrodynamically making (taken as a process of electrodeposition; see Coffee RA, pages 9-10, in particular) fiber mats for use **in treating wounds or burns** (see Coffee RA, abstract, and claims 1-5, in particular). Among the various fibers that may be used is **fibrin**, which may be formed *in situ* by action of thrombin on fibrinogen (see Coffee RA, page 28, claims 20, 25-26, 36). A wide range of biologically active ingredients may be incorporated, including nucleic acids, growth factors, therapeutic agents, cells, etc. (see Coffee RA, pages 5-6, in particular). The fiber mat may be incorporated into conventional bandages and wound dressings (see Coffee RA, pages 6 and 17, in particular), thus the product produced encompasses electrodeposited fibrin matrix with cells. In addition, Coffee RA discloses the fact that the liquid used for electrodeposition may “comprise a solution, suspension, microsuspension, emulsion...which may contain an active components or components (see Coffee RA, page 5, 2nd and 3rd paragraphs, pages 6-7, 22-23 and 28, in particular), which are disclosed as encompassing various pharmaceutical compounds such as drugs, including “biological products such as cells, and cytokines” (see page 5, 3rd paragraph, in particular), wherein the cells may be interspersed in or between layers of the electrodeposited composition (see page 23, 2nd paragraph, in particular).

Coffee RA (US 2001/0003148; IDS) discloses an electrohydrodynamic method of producing mats from suitable fibers, which process is reasonably expected to produce electrodeposited matrix with cells. Specifically, fibrin is produced (paragraph 0017, 0085, claim 26 and claim 36). The fibrin fibers may comprise additional biologically active material (paragraph 0021). Coffee RA (US 6,252,129) discloses an electrohydrodynamic method of producing mats from suitable fibers. Specifically, fibrin is produced (column 3, line 43; column 14, line 12). The fibers may comprise additional biologically active material (see, paragraph bridging columns 3-4).

Even though, an electrodeposited fibrin matrix comprising cells is not explicitly exemplified by the referenced inventions of Coffee RA (WO 98/03267; IDS, citation # 70),

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Coffee RA (US 2001/0003148; IDS, citation # 1), and Coffee RA (US 6,252,129; IDS, citation No. 46), this product is clearly envisioned by the reference disclosures.

Given the fact that Coffee RA (WO 98/03267, IDS) discloses that a product as claimed, i.e. an electrodeposited fibrin matrix is made using solutions or suspensions comprising **fibrinogen and/or thrombin** (see claims 15-20, 26, 36-38, in particular), wherein the solutions or liquids can be further added with **polymers or cells and/or other biological components** such as growth factors, drugs, peptides, etc (see Coffee RA, discussion above), and electrodeposited on a desired surface to produce a fibrin **mat or web** (i.e. fibrin matrix) which can be interspersed with the cells between the layers (see Coffee RA, page 23, 2nd paragraph, in particular), it would have been clearly obvious to a person of ordinary skill in the tissue engineering art to incorporate cells (such as skin cells) and/or other biological components (such as drugs, hormones, peptides, etc.) in the fibrin matrix in order to provide an electrodeposited fibrin matrix with cells having the benefits of incorporated biological agents such as drugs, for example in the form of a superior wound dressing or covering, or **skin substitute**, as exemplified by Coffee RA, WO 98/03267; see abstract, pages 4-7, pages 17-19, pages 22-23 and 28; and claims, in particular.

However, a product as claimed i.e. an electrodeposited fibrin matrix with cells, wherein a **cross-linking agent** is added to the electrodeposited fibrin matrix, though implicitly suggested (see Coffee WO 98/03267; page 17, last paragraph, in particular for creating a product in the form of a network of crossing or interlinking fibers to result in web or mat), is not explicitly taught by the cited prior art references (Coffee RA, as discussed above).

Weinberg [A] discloses use of cross-linking agents in the process of making fibrin-collagen tissue equivalents that also comprise cells (see Weinberg, abstract, summary of the invention, column 4, 1st paragraph, columns 5-7, and claims, in particular), wherein the cross-linking agent such as Factor XIII is used (see column 7, 2nd paragraph and example 2, in particular) to provide strength to the fibrin-collagen tissue equivalents by cross-linking or chemically stabilizing fibrin and collagen (a structural protein ubiquitously present in and around mammalian cells and tissues) lattice that contains mammalian cells such as fibroblast cells (see column 6, in particular).

Thus, it would have been obvious to a person of ordinary skill in the clinical art (at the time this invention was made) to include a cross-linking agent (as explicitly taught by Weinberg [A]) in the process as disclosed by Coffee RA (see discussion above) to achieve a better and tougher electrodeposited fibrin matrix containing cells, the benefit which is desired and explicitly disclosed by Weinberg et al (see column 6, in particular). An artisan of ordinary skill in the clinical art would be motivated, and would have had a reasonable expectation of success in including a cross-linking agent that is added to the product disclosed by Coffee RA, as Weinberg clearly discloses the benefits associated with the addition of such cross-linking agents as factor XIII (i.e. for achieving superior strength of the tissue equivalents comprising fibrin).

The process limitations as recited in instant claims, wherein the cells are delivered to the matrix during fabrication of the electrodeposited fibrin matrix, wherein the cells are suspended in a solution comprising molecules capable of forming fibrin during delivery to the matrix, or wherein the cells are entrapped within the matrix during fabrication of the electrodeposited fibrin

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matrix, wherein the cells are suspended in a fibrinogen solution during delivery to the matrix (see instant claims 1, and 21), are disclosed by Coffee RA, as it describes the same process steps of electrodeposition of materials in liquid, solution or suspension form (containing polymers, and/or cells and other beneficial biological components such as drugs, hormones, etc.) in order to obtain the electrodeposited fibrin matrix or mat containing cells. In the absence of any evidence to contrary, the “electrodeposited fibrin matrix with cells” product as explicitly suggested by the referenced invention of Coffee RA (WO 98/03267, US 2001/0003148), and US 6,252,129 is deemed to be substantially similar if not the same as the claimed product. In addition, the inclusion of a cross-linking agent in order to provide strength (by cross-linking fibrin and collagen fibers) to the product obtained (i.e. the electrodeposited fibrin matrix containing cells as discussed above) would have been an obvious step in the process of making such tissue equivalents or products, as disclosed by Coffee RA, in view of the disclosure provided by the cited prior art reference of Weinberg.

The newly added limitation of claims 1 and 21 “**upon a target that contains calcium**” is met by the cited prior art reference of Coffee RA (WO 98/03267, IDS), wherein the Coffee discloses the application or electrodeposition of fibrin “upon a target that contains calcium” such as to internal surfaces of an animal skin (animal body taken as a target containing calcium), for example “in the care or treatment of wounds or burns” (see Coffee, abstract, page 1, 1st paragraph, in particular), or to a body cavity (see Coffee, page 2, 2nd to 4th paragraphs; and page 5, 1st paragraph, in particular). An artisan of ordinary skill in the clinical art would have had a reasonable understanding for the fact that animal skin surface with burns or wound contains calcium ions (i.e. various forms of free and protein-associated calcium contained in cells as well as body fluids such as plasma/lymph), and will act as a “target” that will stabilize the electrodeposited fibrin matrix (with or without added cells). Also, as evidenced by the cited prior art of Weinberg [A] that discloses the fact that calcium ions are necessary for the formation of fibrin from fibrinogen in the presence of thrombin (see column 6, first and last paragraphs, in particular), and can be conveniently provided in various forms or at various steps in the process, as per need or suitability. Thus, an artisan of ordinary skill in the clinical and tissue regeneration art would be motivated to use a “target that contains calcium” (i.e. a surface that contains calcium), for example, a tissue surface such as skin wound or burn, etc. that will provide calcium ions that are known in the art to accelerate and/or activate the fibrin matrix formation from fibrinogen solution in the presence of thrombin (or an analog thereof) in order to further stabilize (as fibrin is known to clot in the presence of the calcium ion; see Weinberg, column 6, lines 6-9, in particular) the electrodeposited fibrin matrix containing cells, the fabrication of which is explicitly suggested by Coffee.

Thus, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the tissue engineering or clinical art at the time the claimed invention was made.

As per MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a

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clear definition in the specification. *In re Zletz*, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

As per MPEP 2144.06, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

As per MPEP 2144.04, Ex parte Rubin, 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Response to Applicant's Arguments

Applicant's arguments filed with the office on November 17th 2008 (see response, pages 5, in particular) with respect to claims 1, 4, 5 and 21 (as they pertain to the prior art rejections of record) have been considered but are not found to be persuasive for the following reasons of record:

"Claims 1, 4, 5 and 21 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Coffee RA (WO 98/03267), in view of Coffee RA (US 2001/0003148), in further view of Coffee RA (US 6,252,129), and further in view of Weinberg (US 4,837,379).

As amended, independent claim 1 from which claims 4 and 5 depend and 21 require that the fibrin is fabricated using a target that contains calcium. None of the cited references, each alone or in any combination teach or suggest the instant claimed subject matter. Accordingly, Applicants respectfully request that the rejection be withdrawn."

In response, it is noted that the newly added limitation of **"upon a target that contains calcium"** is fully met by the prior art cited in the obviousness rejection of record (see also rejection above) as Coffee (WO 98/03267, IDS) discloses the application or electrodeposition of fibrin "upon a target that contains calcium" such as to an internal surface of an animal skin or body (animal body taken as "a target that contains calcium"), for example "in the care or treatment of wounds or burns" (see Coffee, abstract, page 1, 1st paragraph, in particular), or to a body cavity (see Coffee,

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page 2, 2nd to 4th paragraphs; and page 5, 1st paragraph, in particular). In addition, role of calcium in the activation, formation and stabilization of fibrin matrix (i.e. formed from fibrinogen) is well known in the art, as evidenced by the cited disclosure of Weinberg and therefore an artisan of ordinary skill in the clinical and tissue regeneration art would have fully contemplated at the time this invention was made, and would have been motivated by the fact that a “target” containing calcium (such as a body tissue, for example, skin wounds, burns, etc.) would reasonably stabilize the electrodeposited fibers of fibrin (with or without added cells or other compatible biological materials) and thus will provide added benefits in the fabrication and stabilization of an “electrodeposited fibrin matrix with cells”, which has been clearly contemplated and suggested by the cited disclosure of Coffee. The prior art rejection of record is therefore properly made and maintained.

Conclusion

NO claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA K. SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Satyendra K. Singh/
Examiner, Art Unit 1657

/Irene Marx/
Primary Examiner
Art Unit 1651